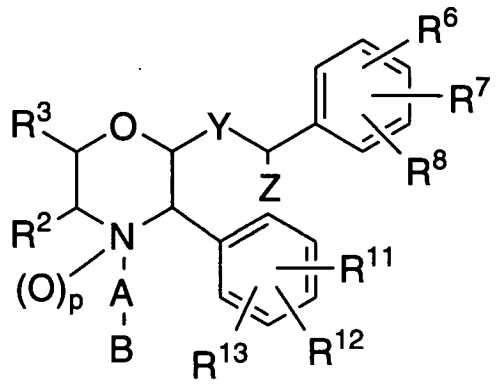
-- 31. A compound of structural formula:



or a pharmaceutically acceptable salt thereof, wherein:

R^2 and R^3 are independently selected from the group consisting of:

(1) hydrogen,

(2) C_{1-6} alkyl, unsubstituted or substituted with one or more of the substituents selected from:

(a) hydroxy,

(b) oxo,

(c) C_{1-6} alkoxy,

(d) phenyl-C_{1-3} alkoxy,

(e) phenyl,

(f) -CN,

(g) halo,

(h) $-NR^9R^{10}$, wherein R^9 and R^{10} are independently selected from:

(i) hydrogen,

(ii) C_{1-6} alkyl,

(iii) hydroxy-C_{1-6} alkyl, and

(iv) phenyl,

(i) $-NR^9COR^{10}$,

(j) $-NR^9CO_2R^{10}$,

(k) $-CONR^9R^{10}$,

(l) $-COR^9$, and
(m) $-CO_2R^9$;

(3) C_{2-6} alkenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
(a) hydroxy,
(b) oxo,
(c) C_{1-6} alkoxy,
(d) phenyl-C_{1-3} alkoxy,
(e) phenyl,
(f) -CN,
(g) halo,
(h) $-CONR^9R^{10}$,
(i) $-COR^9$,
(j) $-CO_2R^9$;
(4) C_{2-6} alkynyl;
(5) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
(a) hydroxy,
(b) C_{1-6} alkoxy,
(c) C_{1-6} alkyl,
(d) C_{2-5} alkenyl,
(e) halo,
(f) -CN,
(g) $-NO_2$,
(h) $-CF_3$,
(i) $-(CH_2)_m-NR^9R^{10}$, wherein m is 0, 1 or 2,
(j) $-NR^9COR^{10}$,
(k) $-NR^9CO_2R^{10}$,
(l) $-CONR^9R^{10}$,
(m) $-CO_2NR^9R^{10}$,
(n) $-COR^9$, and

(o) $-CO_2R^9$;

or the groups R^2 and R^3 are joined together to form a carbocyclic ring selected from the group consisting of:

(a) cyclopentyl,
(b) cyclohexyl,
(c) phenyl,

and wherein the carbocyclic ring is unsubstituted or substituted with one or more substituents selected from:

(i) C_{1-6}alkyl,
(ii) C_{1-6}alkoxy,
(iii) $-NR^9R^{10}$,
(iv) halo, and
v) trifluoromethyl;

or the groups R^2 and R^3 are joined together to form a heterocyclic ring selected from the group consisting of:

(a) pyrrolidinyl,
(b) piperidinyl,
(c) pyrrolyl,
(d) pyridinyl,
(e) imidazolyl,
(f) furanyl,
(g) oxazolyl,
(h) thienyl, and
(i) thiazolyl,

and wherein the heterocyclic ring is unsubstituted or substituted with one or more substituent(s) selected from:

(i) C_{1-6}alkyl,
(ii) oxo,
(iii) C_{1-6}alkoxy,
(iv) $-NR^9R^{10}$,

(v) halo, and
(vi) trifluoromethyl;

R^6, R^7 and R^8 are independently selected from the group consisting of:

(1) hydrogen;
(2) C_{1-6} alkyl, unsubstituted or substituted with one or more of the substituents selected from:
  (a) hydroxy,
  (b) oxo,
  (c) C_{1-6} alkoxy,
  (d) phenyl-C_{1-3} alkoxy,
  (e) phenyl,
  (f) -CN,
  (g) halo,
  (h) $-NR^9R^{10}$,
  (i) $-NR^9COR^{10}$,
  (j) $-NR^9CO_2R^{10}$,
  (k) $-CONR^9R^{10}$,
  (l) $-COR^9$, and
  (m) $-CO_2R^9$;

(3) C_{2-6} alkenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
  (a) hydroxy,
  (b) oxo,
  (c) C_{1-6} alkoxy,
  (d) phenyl-C_{1-3} alkoxy,
  (e) phenyl,
  (f) -CN,
  (g) halo,
  (h) $-CONR^9R^{10}$,
  (i) $-COR^9$, and
  (j) $-CO_2R^9$;

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(4) C_{2-6} alkynyl;

(5) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:

(a) hydroxy,
(b) C_{1-6} alkoxy,
(c) C_{1-6} alkyl,
(d) C_{2-5} alkenyl,
(e) halo,
(f) -CN,
(g) $-NO_2$,
(h) $-CF_3$,
(i) $-(CH_2)_m-NR^9R^{10}$,
(j) $-NR^9COR^{10}$,
(k) $-NR^9CO_2R^{10}$,
(l) $-CONR^9R^{10}$,
(m) $-CO_2NR^9R^{10}$,
(n) $-COR^9$, and
(o) $-CO_2R^9$;

(6) halo,
(7) -CN,
(8) $-CF_3$,
(9) $-NO_2$,
(10) $-SR^{14}$, wherein R^{14} is hydrogen or C_{1-5}alkyl,
(11) $-SOR^{14}$,
(12) $-SO_2R^{14}$,
(13) NR^9COR^{10},
(14) $CONR^9COR^{10}$,
(15) NR^9R^{10},
(16) $NR^9CO_2R^{10}$,
(17) hydroxy,
(18) C_{1-6}alkoxy,
(19) COR^9,

a' until

750

(20) CO_2R^9,
(21) 2-pyridyl,
(22) 3-pyridyl,
(23) 4-pyridyl,
(24) 5-tetrazolyl,
(25) 2-oxazolyl, and
(26) 2-thiazolyl;

R^{11}, R^{12} and R^{13} are independently selected from the definitions of R^6, R^7 and R^8, or -OX;

A is selected from the group consisting of:

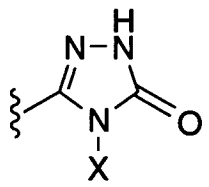
(1) C_{1-6} alkyl, unsubstituted or substituted with one or more of the substituents selected from:
  (a) hydroxy,
  (b) oxo,
  (c) C_{1-6} alkoxy,
  (d) phenyl-C_{1-3} alkoxy,
  (e) phenyl,
  (f) -CN,
  (g) halo, wherein halo is fluoro, chloro, bromo or iodo,
  (h) $-NR^9R^{10}$,
  (i) $-NR^9COR^{10}$,
  (j) $-NR^9CO_2R^{10}$,
  (k) $-CONR^9R^{10}$,
  (l) $-COR^9$, and
  (m) $-CO_2R^9$;

(2) C_{2-6} alkenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
  (a) hydroxy,
  (b) oxo,

(c) C_{1-6} alkoxy,
(d) phenyl-C_{1-3} alkoxy,
(e) phenyl,
(f) -CN,
(g) halo,
(h) $-CONR^9R^{10}$,
(i) $-COR^9$, and
(j) $-CO_2R^9$; and

(3) C_{2-6} alkynyl;

B is a heterocycle, wherein the heterocycle is selected from the group consisting of: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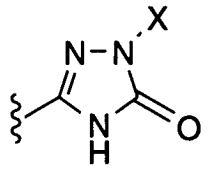
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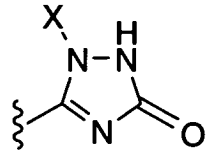
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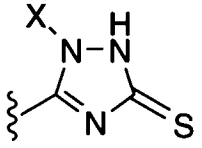
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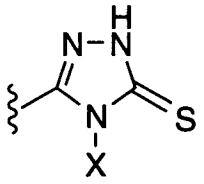
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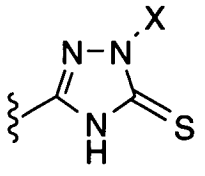
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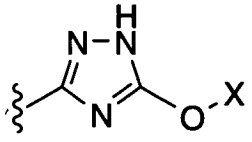
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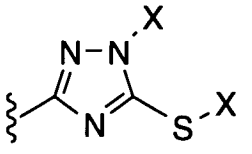
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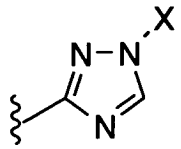
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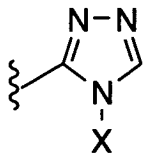
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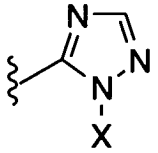
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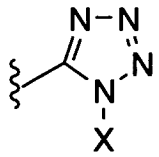
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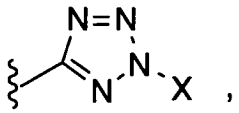
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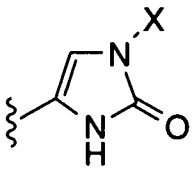
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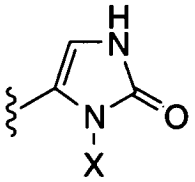
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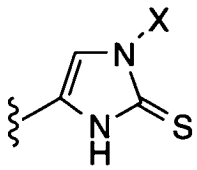
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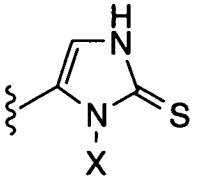
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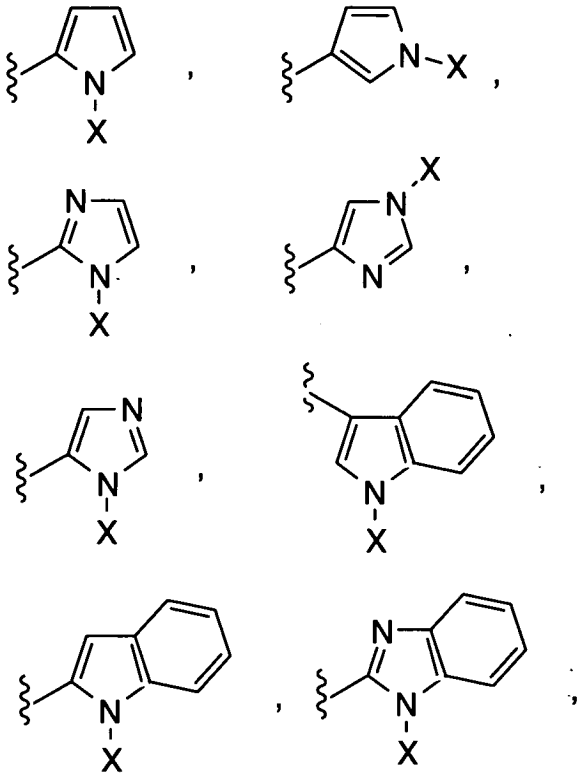


and wherein the heterocycle is substituted in addition to -X with one or more substituent(s) selected from:

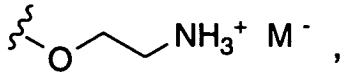
(i) hydrogen;
(ii) C_{1-6} alkyl, unsubstituted or substituted with halo, $-CF_3$, $-OCH_3$, or phenyl,
(iii) C_{1-6} alkoxy,
(iv) oxo,
(v) hydroxy,
(vi) thioxo,
(vii) $-SR^9$,
(viii) halo,
(ix) cyano,
(x) phenyl,
(xi) trifluoromethyl,
(xii) $-(CH_2)_m-NR^9R^{10}$,
(xiii) $-NR^9COR^{10}$,

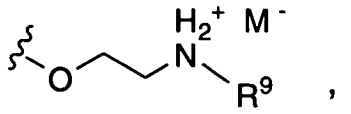
(xiv) $-CONR^9R^{10}$,
(xv) $-CO_2R^9$, and
(xvi) $-(CH_2)_m-OR^9$;

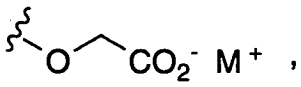
p is 0 or 1;

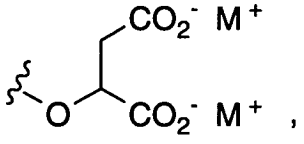
X is selected from:

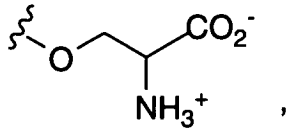
(a) $-PO(OH)O^- \cdot M^+$, wherein M^+ is a pharmaceutically acceptable monovalent counterion,
(b) $-PO(O^-)_2 \cdot 2M^+$,
(c) $-PO(O^-)_2 \cdot D^{2+}$, wherein D^{2+} is a pharmaceutically acceptable divalent counterion,
(d) $-CH(R^4)-PO(OH)O^- \cdot M^+$, wherein R^4 is hydrogen or C_{1-3} alkyl,
(e) $-CH(R^4)-PO(O^-)_2 \cdot 2M^+$,
(f) $-CH(R^4)-PO(O^-)_2 \cdot D^{2+}$,
(g) $-SO_3^- \cdot M+$,
(h) $-CH(R^4)-SO_3^- \cdot M^+$,
(i) $-CO-CH_2CH_2-CO_2^- \cdot M^+$,
(j) $-CH(CH_3)-O-CO-R^5$, wherein R^5 is selected from the group consisting of:

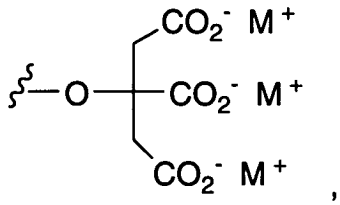
(i)  ,

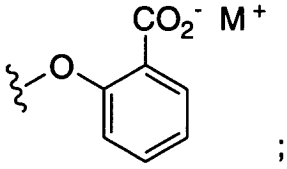
(ii)  ,

(iii)  ,

(iv)  ,

(v)  ,

(vi)  ,

(vii)  ; and

(k) hydrogen, with the proviso that if p is 0 and none of R^{11}, R^{12} or R^{13} are -OX, then X is other than hydrogen;

Y is selected from the group consisting of:

(1) a single bond,
(2) -O-,
(3) -S-,
(4) -CO-,
(5) $-CH_2-$,
(6) $-CHR^{15}-$, and
(7) $-CR^{15}R^{16}-$, wherein R^{15} and R^{16} are independently selected from the group consisting of:
  (a) C_{1-6} alkyl, unsubstituted or substituted with one or more of the substituents selected from:
    (i) hydroxy,
    (ii) oxo,
    (iii) C_{1-6} alkoxy,
    (iv) phenyl-C_{1-3} alkoxy,
    (v) phenyl,
    (vi) -CN,
    (vii) halo,
    (viii) $-NR^9R^{10}$,
    (ix) $-NR^9COR^{10}$,
    (x) $-NR^9CO_2R^{10}$,
    (xi) $-CONR^9R^{10}$,
    (xii) $-COR^9$, and
    (xiii) $-CO_2R^9$;

  (b) phenyl, unsubstituted or substituted with one or more of the substituent(s) selected from:
    (i) hydroxy,
    (ii) C_{1-6} alkoxy,
    (iii) C_{1-6} alkyl,
    (iv) C_{2-5} alkenyl,
    (v) halo,
    (vi) -CN,

(vii) $-NO_2$,
(viii) $-CF_3$,
(ix) $-(CH_2)_m-NR^9R^{10}$,
(x) $-NR^9COR^{10}$,
(xi) $-NR^9CO_2R^{10}$,
(xii) $-CONR^9R^{10}$,
(xiii) $-CO_2NR^9R^{10}$,
(xiv) $-COR^9$, and
(xv) $-CO_2R^9$;

Z is selected from:

(1) hydrogen,
(2) C_{1-6} alkyl, and
(3) hydroxy, with the proviso that if Y is -O-, then Z is other than hydroxy,
and with the further proviso that if Y is $-CHR^{15}-$, then Z and R^{15} may be joined together to form a double bond between the two carbon atoms.

~~32~~ 2. The compound of Claim ~~31~~ 1 wherein:

R^2 and R^3 are independently selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) C_{2-6} alkenyl, and
(4) phenyl;

R^6, R^7 and R^8 are independently selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) fluoro,
(4) chloro,
(5) bromo,
(6) iodo, and
(7) $-CF_3$;

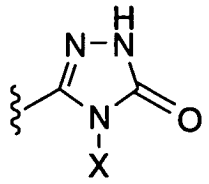
R^{11}, R^{12} and R^{13} are independently selected from the group consisting of:

(1) fluoro,
(2) chloro,
(3) bromo, and
(4) iodo;

A is unsubstituted C_{1-6} alkyl;

B is selected from the group consisting of:

T2600X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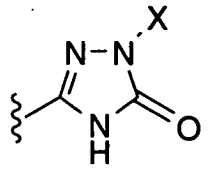
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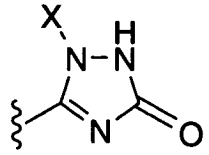
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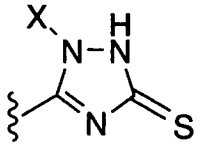
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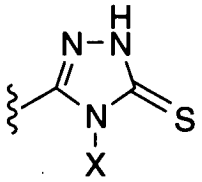
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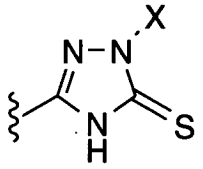
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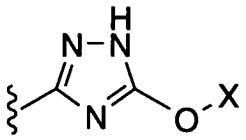
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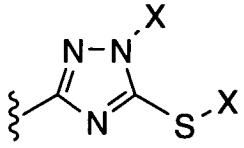
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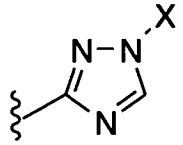
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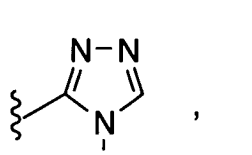
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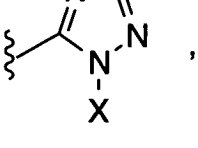
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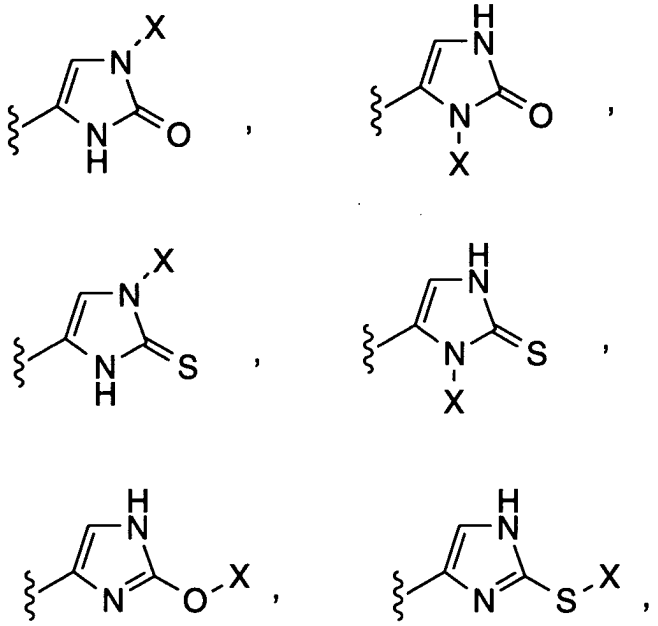


p is 0;

X is selected from:

(a) $-PO(OH)O^- \cdot M^+$, wherein M^+ is a pharmaceutically acceptable monovalent counterion,

(b) $-PO(O^-)_2 \cdot 2M^+$,

(c) $-PO(O^-)_2 \cdot D^{2+}$, wherein D^{2+} is a pharmaceutically acceptable divalent counterion,

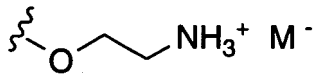
(d) $-CH(R^4)-PO(OH)O^- \cdot M^+$, wherein R^4 is hydrogen or methyl,

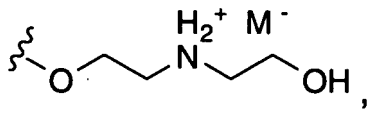
(e) $-CH(R^4)-PO(O^-)_2 \cdot 2M^+$,

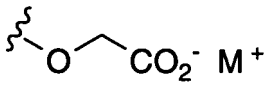
(f) $-CH(R^4)-PO(O^-)_2 \cdot D^{2+}$,

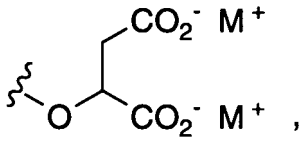
(g) $-CO-CH_2CH_2-CO_2^- \cdot M^+$,

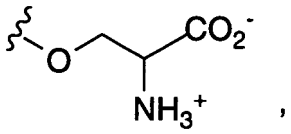
(h) $-CH(CH_3)-O-CO-R^5$, wherein R^5 is selected from the group consisting of:

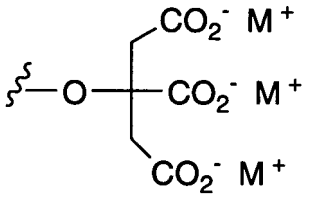
(i)  ,

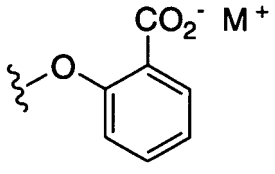
(ii)  ,

(iii)  ,

(iv)  ,

(v)  ,

(vi)  ,

(vii)  ; and

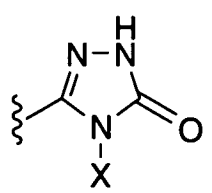
Y is -O-;
Z is hydrogen or C1-4 alkyl.

33. The compound of Claim 31 wherein Z is C_{1-4} alkyl.

34. The compound of Claim 31 wherein Z is $-CH_3$.

35. The compound of Claim 31 wherein A is $-CH_2-$ or $-CH(CH_3)-$.

36. The compound of Claim 31 wherein -B is selected from the group consisting of: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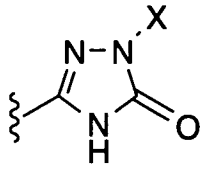
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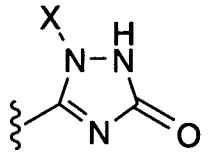
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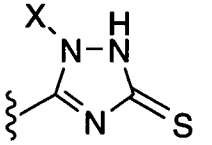
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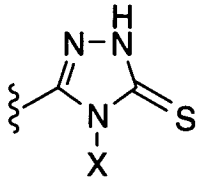
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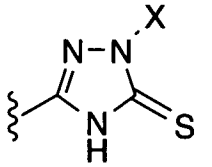
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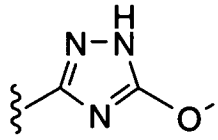
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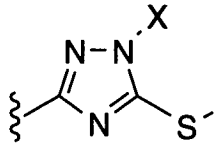
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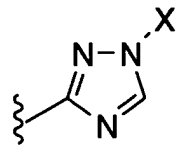
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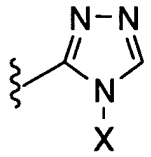
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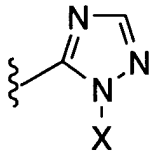
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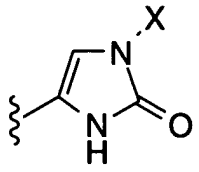
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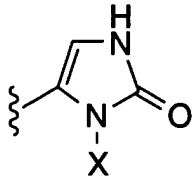
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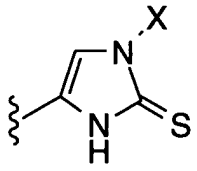
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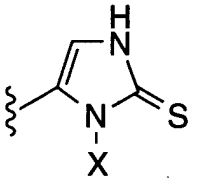
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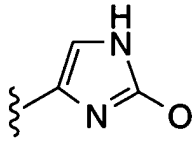
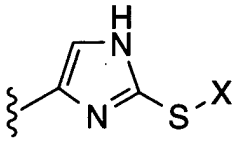

, and

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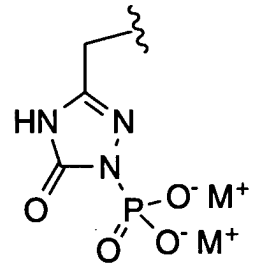
37. The compound of Claim 31 wherein -A-B is selected from the group consisting of:



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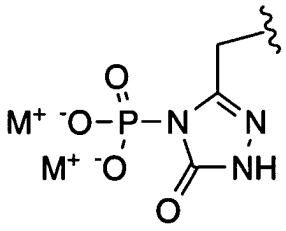

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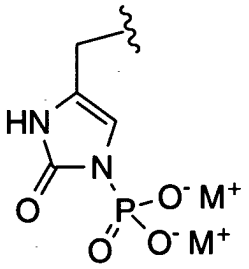
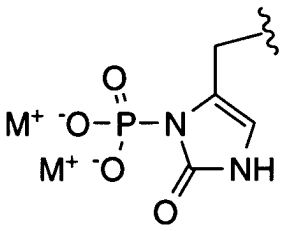


, and



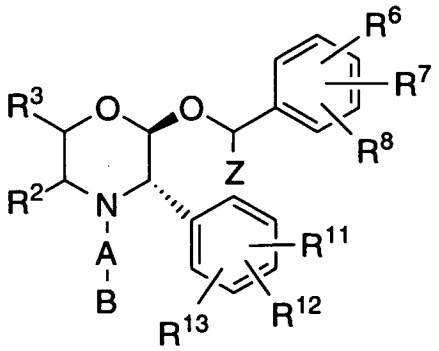
.

38. The compound of Claim 31 wherein X is selected from the group consisting of:

(a) $-PO(O^-)_2 \cdot 2M^+$, wherein M^+ is a pharmaceutically acceptable monovalent counterion, and

(b) $-PO(O^-)_2 \cdot D^{2+}$, wherein D^{2+} is a pharmaceutically acceptable divalent counterion.

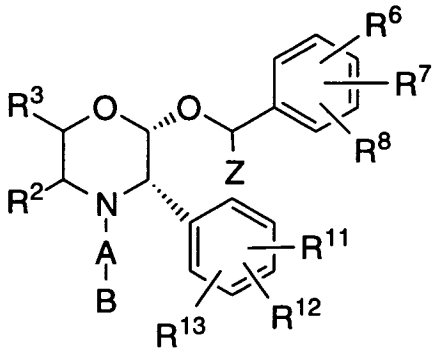
39. The compound of Claim 31 of the structural formula II:



II

or a pharmaceutically acceptable salt thereof, ~~wherein R2, R3, R6, R7, R8, R11, R12, R13, A, B and Z are as defined in Claim 1.~~

40. The compound of Claim 41 of the structural formula III:



III

or a pharmaceutically acceptable salt thereof, ~~wherein R2, R3, R6, R7, R8, R11, R12, R13, A, B, and Z are as defined in Claim 1.~~

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41. A compound which is selected from the group consisting of:

(1) 2-(S)-(3,5-bis(trifluoromethyl)benzyloxy)-3-(S)-phenyl-4-(3-(5-oxo-1H,4H-1,2,4-triazolo)methyl)morpholine N-oxide;

(2) 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)-phenyl-4-(3-(4-monophosphoryl-5-oxo-1H-1,2,4-triazolo)methyl)morpholine;

(3) 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)-phenyl-4-(3-(1-monophosphoryl-5-oxo-1H-1,2,4-triazolo)methyl)morpholine;

(4) 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)-phenyl-4-(3-(2-monophosphoryl-5-oxo-1H-1,2,4-triazolo)methyl)morpholine;

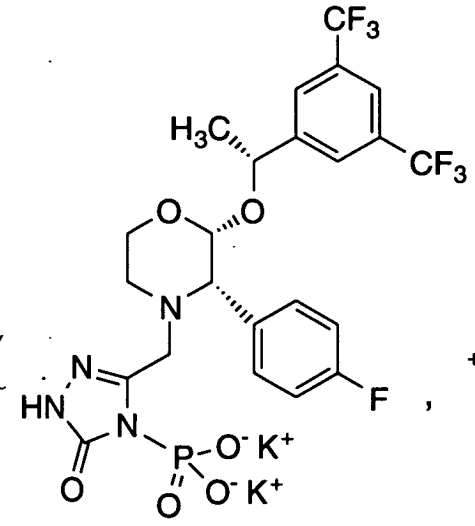
(5) 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)-phenyl-4-(3-(5-oxyphosphoryl-1H-1,2,4-triazolo)-methyl)morpholine;

(6) 2-(S)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)-phenyl-4-(3-(1-phosphoryl-5-oxo-4H-1,2,4-triazolo)methyl)morpholine;

or a pharmaceutically acceptable salt thereof.

42. The compound of Claim 41 wherein the pharmaceutically acceptable salt is the bis(N-methyl-D-glucamine) salt.

~~43~~ 13. A compound which is selected from the group consisting of:



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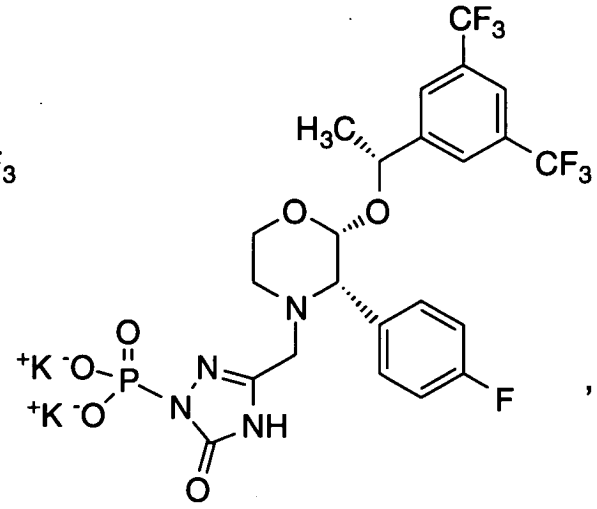

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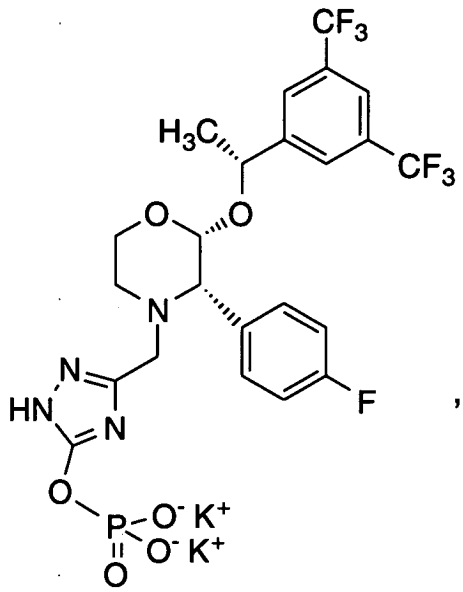

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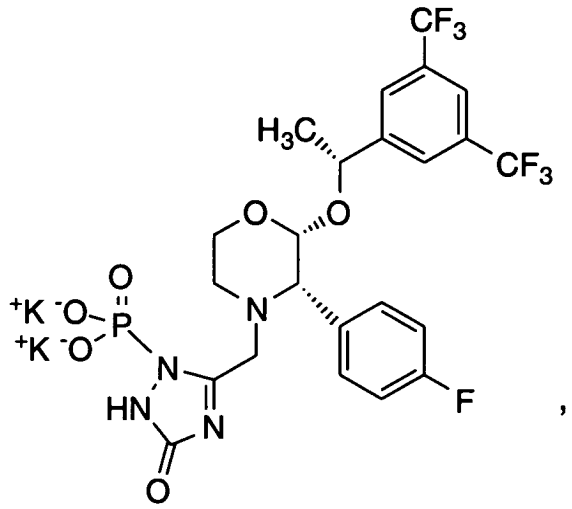

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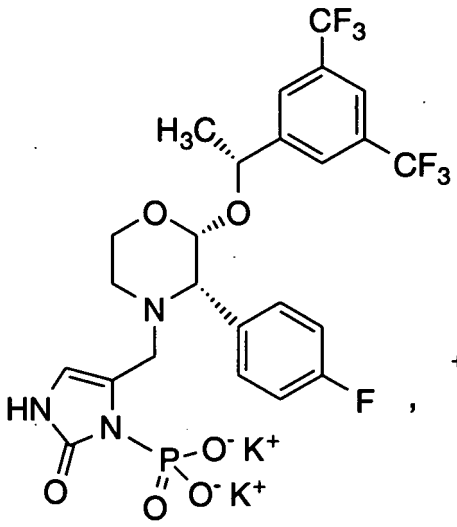

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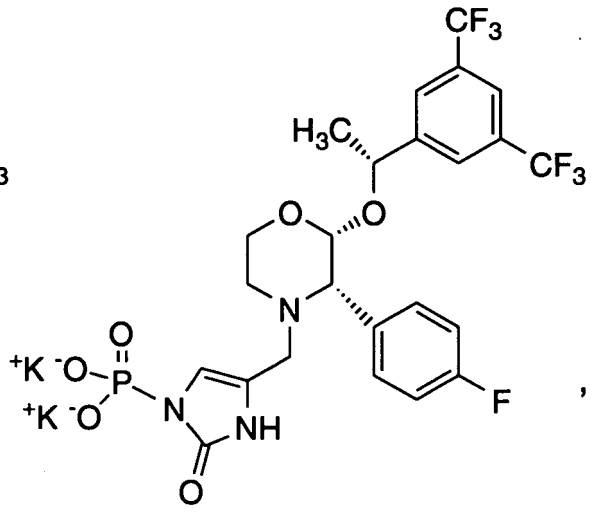

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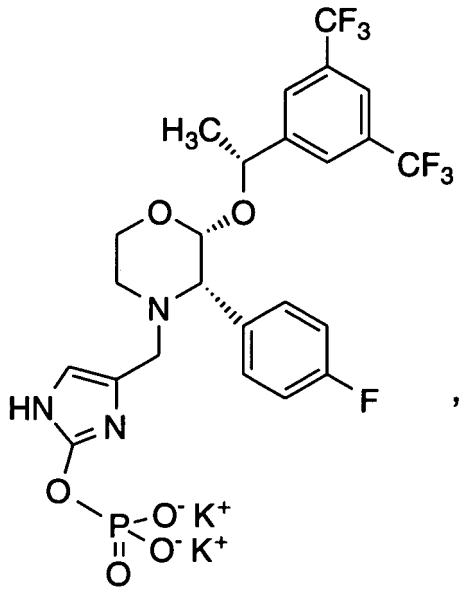


,

wherein K^+ is a pharmaceutically acceptable counterion.

769

14. A compound which is:

2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl-4-(3-(1-phosphoryl-5-oxo-4H-1,2,4-triazolo)methylmorpholine;

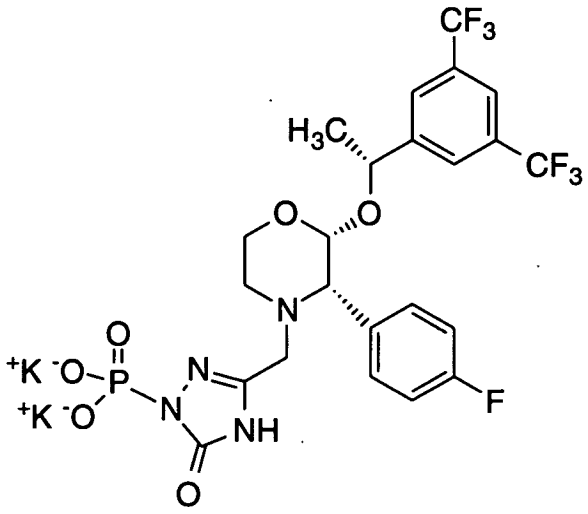
or a pharmaceutically acceptable salt thereof.

15. The compound of Claim 14 wherein the pharmaceutically acceptable salt is the bis(N-methyl-D-glucamine) salt.

16. A compound which is

2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl-4-(3-(1-phosphoryl-5-oxo-4H-1,2,4-triazolo)methylmorpholine, bis(N-methyl-D-glucamine).

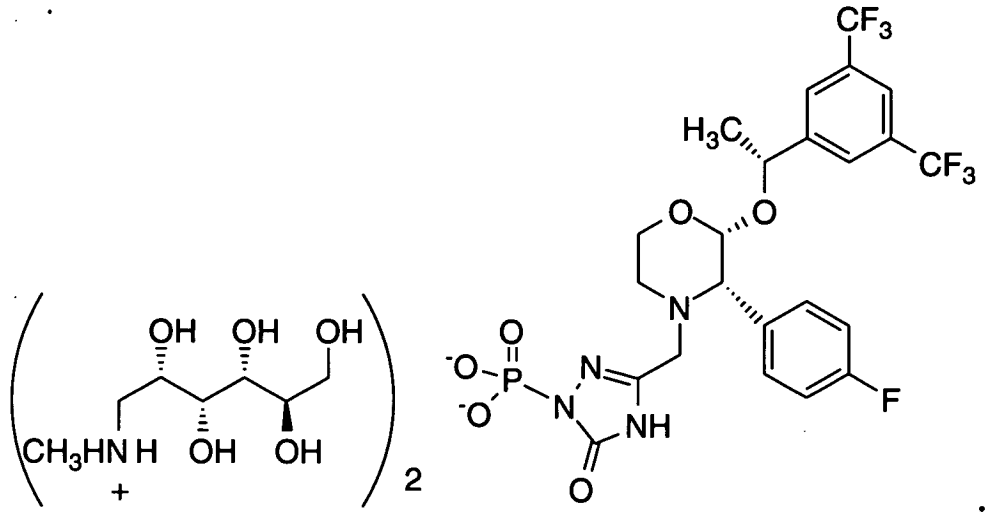
17
~~47~~. A compound which is:



wherein K^+ is a pharmaceutically acceptable counterion.

18 17
~~48~~. The compound of Claim ~~47~~ wherein K^+ is N-methyl-D-glucamine.

19
~~49~~. A compound which is:

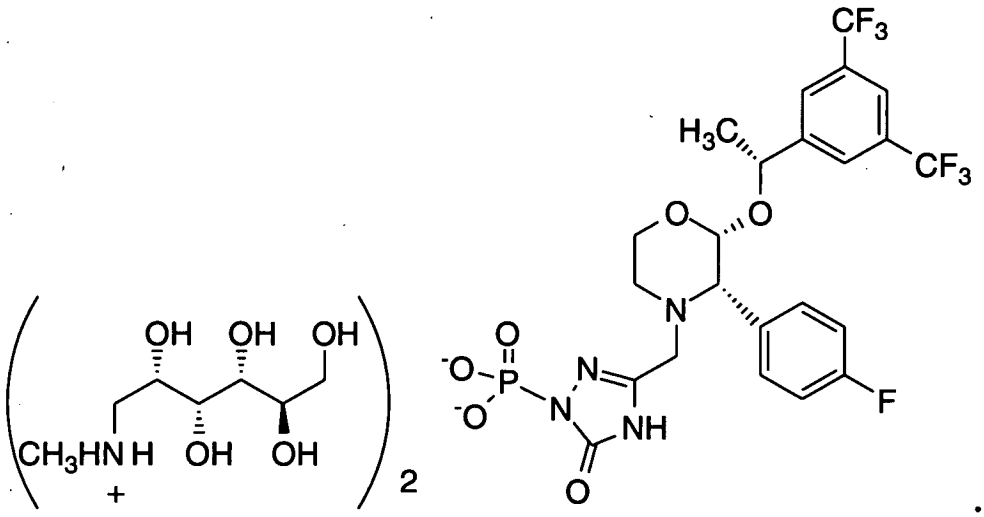


50. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an effective amount of the compound of Claim 1.

51. The pharmaceutical composition of Claim 50 wherein the pharmaceutically acceptable carrier comprises water.

52. The pharmaceutical composition of Claim 50 wherein the pharmaceutically acceptable carrier comprises a physiologically acceptable saline solution.

53. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an effective amount of a compound which is:



54. A method for antagonizing the effect of substance P at its receptor site or for the blockade of neurokinin-1 receptors in a mammal which comprises the administration to the mammal of the compound of Claim 31 in an amount that is effective for antagonizing the effect of substance P at its receptor site or for the blockade of neurokinin-1 receptors in the mammal.

55. A method of treating or preventing pain or nociception which comprises the administration to the mammmal of an effective amount of the compound of Claim 31.

56. A method of treating or preventing a condition selected from the group consisting of: diabetic neuropathy; peripheral neuropathy; AIDS related neuropathy; chemotherapy-induced neuropathy; and neuralgia, in a mammal in need thereof which comprises the administration to the mammal of an effective amount of the compound of Claim 31.

57. A method for the treatment or prevention of asthma in a mammal in need thereof which comprises the administration to the mammal of an effective amount of the compound of Claim 31, either alone or in combination with a neurokinin-2 receptor antagonist or with a β_2-adrenergic receptor agonist.

58. A method for the treatment of cystic fibrosis in a mammal in need thereof which comprises the administration to the mammal of an effective amount of the compound of Claim 31.

59. A method for the treatment or prevention of arthritis in a mammal in need thereof which comprises the administration to the mammal of an effective amount of the compound of Claim 31.

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